## REMARKS

By the foregoing Amendment, Claims 49, 53-56, 59-64, 66, 68, 69, 71, 72, 73, 75, 76, 77, 79-82 have been cancelled. Claim 83 has been amended and new claims 84-100 have been added. Entry of the Preliminary Amendment and favorable consideration thereof is earnestly requested.

In the Final Official Action dated May 13, 2004, the Examiner maintained the previous rejection of all claims as being unpatentable for lack of enablement. Applicant respectfully requests that the Examiner reconsider this rejection in view of the above Amendments and the below Remarks.

The present invention is directed to agents such as Ctx, Etx, CtxB, and EtxB which are identified and employed to treat allergic and/or hypersensitivity conditions. Claim 83 specifies the Type I allergies as being only those that are IgE mediated. Claims 89 and 95 further specify the allergic condition as IgE mediated Type I allergies, and specifically excluding non-IgE mediated insect bite allergies, dietary allergies and drug allergies.

No new matter is added by this amendment, and the Applicant directs the examiner's attention to the support in the description located on page 1, lines 24 to 25 of WO 99/34817 (application as published). See also, Page 10, line 18 and page 14, lines 20 to 25.

Applicant respectfully submits that the specification enables the amended claims for the following reasons. Reconsideration is urged.

Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill

of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. See *In re Wands* (858 F.2d 731 (Fed.Cir.1988).

First, Applicant has amended the claims to EtxB agent and by defining the Type I allergies as being only those that are IgE mediated. Thus the breadth of the amended claims has been narrowed.

Second, a requirement for working examples of each and every IgE mediated Type I allergy in light of data for asthma, is not necessary for one of ordinary skill in the art to practice the claimed invention. It is important to note that the skilled person in this case is one with knowledge of immunology and knowledge of models for study of allergy at the time of filing the application. Thus, the skill level is considerably high. Applicant urges that it is sufficient to provide an example of the invention for only one of the diseases in the group, and that the information in the application as filed provides the necessary enablement across the full scope of Type I allergies that are IgE mediated. This is confirmed by the declaration of Neil Williams dated June 13, 2003. There, it can be seen in Figures 3, 4 and 6 that treatment with EtxB reduces IgE levels and associated IL-4 in a model for asthma and allergic rhinitis which are Type I allergies that are IgE mediated. The results further demonstrate that coadministration of EtxB with an antigen/allergen such as OVA, where the EtxB and the OVA are not conjugated, also reduce IgE levels.

Third, the application as filed provides a person of ordinary skill in the art with sufficient guidance to use the known models and materials to work the invention – see pages 32, line 11 to page 35 line 14 of WO 99/34817. One of ordinary skill in the art would be aware of how the models are to be used in the study of allergy. Any additional experimentation needed by one of ordinary skill in the art would not require any inventive skill given the teaching and guidance in the application as filed. At the time of filing, the skilled person's knowledge was that the OVA mouse model was the accepted model for the study of asthma and allergic rhinitis. The skilled person would also be

aware that these are IgE mediated Type I allergies and that the treatment with EtxB can reasonably be extended to other IgE mediated allergies.

Fourth, In *Wands*, the state of the prior art was mentioned as a factor in determining whether undue experimentation is required to practice the claimed invention. Thus, knowledge gained subsequent to filing the application cannot be considered within the knowledge or contemplation of the person skilled in the art at the time of filing the application. The Examiner has cited three new document; Kagan published February 2003; Wiedermann published March 1999; and Herz published March 2004. Thus, the Examiner has cited publications which were available only after the priority date of the application i.e. 9 January 1998. It is respectfully submitted that it is not reasonable to use knowledge gained after the application was filed as to whether the application was enabling at the time of filing.

The fact that there is sufficient enablement for the person skilled in the art at the time of filing the application is shown in the declaration by Neil Williams by working examples in asthma (which also be translated to allergic rhinitis) which is an IgE mediated Type I allergy.

A Type 1 allergy is one where the basis of the reaction is the production of IgE against the allergen. IgE is an antibody that is produced by B cells. The capacity of B cells to produce IgE is directly linked to the levels of IL-4 in the tissue. The primary pathological process involved in all Type 1 allergies is the degranulation of mast cells in the tissues, which results from their having bound IgE, and which leads to acute inflammatory changes and infiltration of eosinophils. Eosinophils are also able to bind to IgE and cause further acute as well as chronic changes as a result of degranulation following allergen binding. These facts are clear in the art and were so prior to the filing date.

The term Type 1 allergy is one which is defined as an IgE mediated response. In the specification, the inventors have demonstrated that EtxB alone, or EtxB admixed with an allergen, is an effective means of lowering levels of allergen specific IgE, decreasing levels of IL-4 and reducing eosinophils infiltration. Clearly, these effects would be desirable outcomes in the treatment of any of the IgE mediated Type 1 allergy as now claimed in the amended claims.

In light of this, Kagan is not relevant to the enablement analysis. Kagan is simply highlighting the lack of available treatment for food allergies. There is clearly an unmet medical need which can now be fulfilled by the present invention. The invention is enabled for Type I allergies which are IgE mediated. If any of the food allergies fit into this category, the invention provides a treatment by reducing the IgE levels amongst other desirable effect.

Furthermore, Weidermann is not relevant to the enablement analysis. This paper was published after the filing date of the application and is therefore not prior art. Second, the publication relates to CtxB conjugated to an antigen. The invention specifically does not relate to conjugated agent and antigen. Thus it is respectfully submitted that it is not reasonable for the Examiner to predict with hind-sight that the unconjugated agent alone or coadminstered with an antigen/allergen according to the invention would not provide a treatment for IgE mediated Type I allergies. At the time of filing the application, the skilled person would not be aware of Weidermann. Therefore, the skilled person would not have any reason to believe that the invention as disclosed and enabled in the application as filed would not work across the full scope of the claims as now amended.

Moreover, Herz is not relevant to the enablement analysis. It is known to all that models for studying a disease can vary. Despite this researchers throughout the scientific community continue to use the models as a basis for determining treatments for a variety of conditions and develop therapeutic treatments for such conditions. In this

case, the basis of the study was to measure the effect of EtxB on IgE response amongst other immunological parameters of a disease state. From the results in the declaration, it is apparent that allergies associated with an IgE response can be treated with EtxB alone or in combination with an antigen/allergen in unconjugated form.

The Examiner has relied heavily on the *In Re Wands* factors in concluding that the specification lacks enablement due to undue experimentation. In *Wands*, the Court actually decided "that the specification was enabling with respect to the claims at issue and found the 'there was considerable direction and guidance' in the specification . . ." See MPEP 2164.01(a). It is respectfully submitted that the instant specification also provides considerable direction and guidance in light of the fact that the independent claims have been amended to Type I allergy that are IgE mediated and the data provided in the declaration under 37 CFR 1.132 filed 6/13/03 by Neil Andrew Williams shows a working example to treating asthma, a Type I allergy. Applicant respectfully submits that the application as filed provides sufficient enablement for a person skilled in the art, the art being immunology and the use of known models for testing allergies, to work the invention as now claimed in the amended claims. The declaration of Neil Williams confirms that the data is derived from using only known technology, guidance to which is provided in the application as filed.

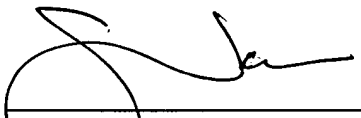
Considering all of the factors, it would not require undue experimentation to treat a variety of Type I allergies that are IgE mediated by practicing the claimed invention, and the efficacy of such treatments would be expected. Thus, Applicants respectfully submit that claims 83-88 are patentable and earnestly solicit allowance of the same.

Claims 89 and 95 further specify the allergic condition as IgE mediated Type I allergies, excluding non-IgE mediated insect bite allergies, dietary allergies and drug allergies. This category specifically excludes the categories of allergies the Examiner has states are not enabled by the specification, thus claims 89-100 are enabled by the specification.

Moreover, claim 95 further specifies that the EtxB agent that binds to GM1 is administered together with an allergen which is not coupled to the EtxB agent. The Examiner has acknowledged that these elements are enabled by the specification, thus there is no basis to objection to claims 95-100.

Accordingly, it is respectfully submitted that claims 83-100 are in order for allowance, and early notice to that effect is respectfully solicited.

Respectfully submitted,



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